

June 8, 1971

Dr. Arthur A. Stein
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The Albany Medical College of Union University
Albany, New York 12208

Dear Dr. Stein,

Thank you for your letter of June 2. What I had in mind was to attempt to set up a bacterial mutation assay as an approach to the identification of biologically active constituents of tobacco juice and tobacco smoke. The confusion that still enshrouds the mechanism of action of smoking on the lung suggests to me that we perhaps ought to spend more effort on some suspected systemic effects, for example, the putative bladder carcinogen in tobacco. I also have in mind the reports on the association of oral cancer with tobacco chewing.

For these effects it would seem at least reasonable that a water-soluble constituent is involved and it is at least possible that appropriate suspicions might be elicited by finding mutagenic activity. I realize that it is also likely that a bladder carcinogen, if there is one, is formed by metabolic conversion within the body as appears to be the case for agents like naphthylamine.

However, we can do the mutation assays so readily but it would seem to be worthwhile testing a small range of tobacco products for the possible exhibition of this kind of activity.

I am not sure how to answer your question about the most appropriate method of preparation and would welcome your own suggestions about this. I suppose I would want, on the one hand, an extract that simulated the consequences of betel-chewing, at least as far as the tobacco component is concerned. On the other hand, I would be looking for condensates of tobacco smoke intended to simulate the input likely to be available for absorption into the circulation.

Whatever we do ~~would~~, of course, want to deal with standardized materials that would allow for the ready replicability of any findings we might encounter. Before going into some possibly more refined analyses perhaps we should do a few preliminary trials with cruder preparations of the kind I mentioned.

Sincerely yours,

Joshua Lederberg
Professor of Genetics

JL/rr

STEIN
D.D.